## 1st INCF Workshop

## on

# Neuroanatomical Nomenclature and Taxonomy

**September 10-11, 2007 - Stockholm, Sweden**

International Neuroinformatics Coordinating Facility

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# 1st INCF Workshop on Neuroanatomical Nomenclature and Taxonomy

**September 10-11, 2007**
**International Neuroinformatics Coordinating Facility Secretariat**
**Stockholm, Sweden**

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## Scientific Organizer

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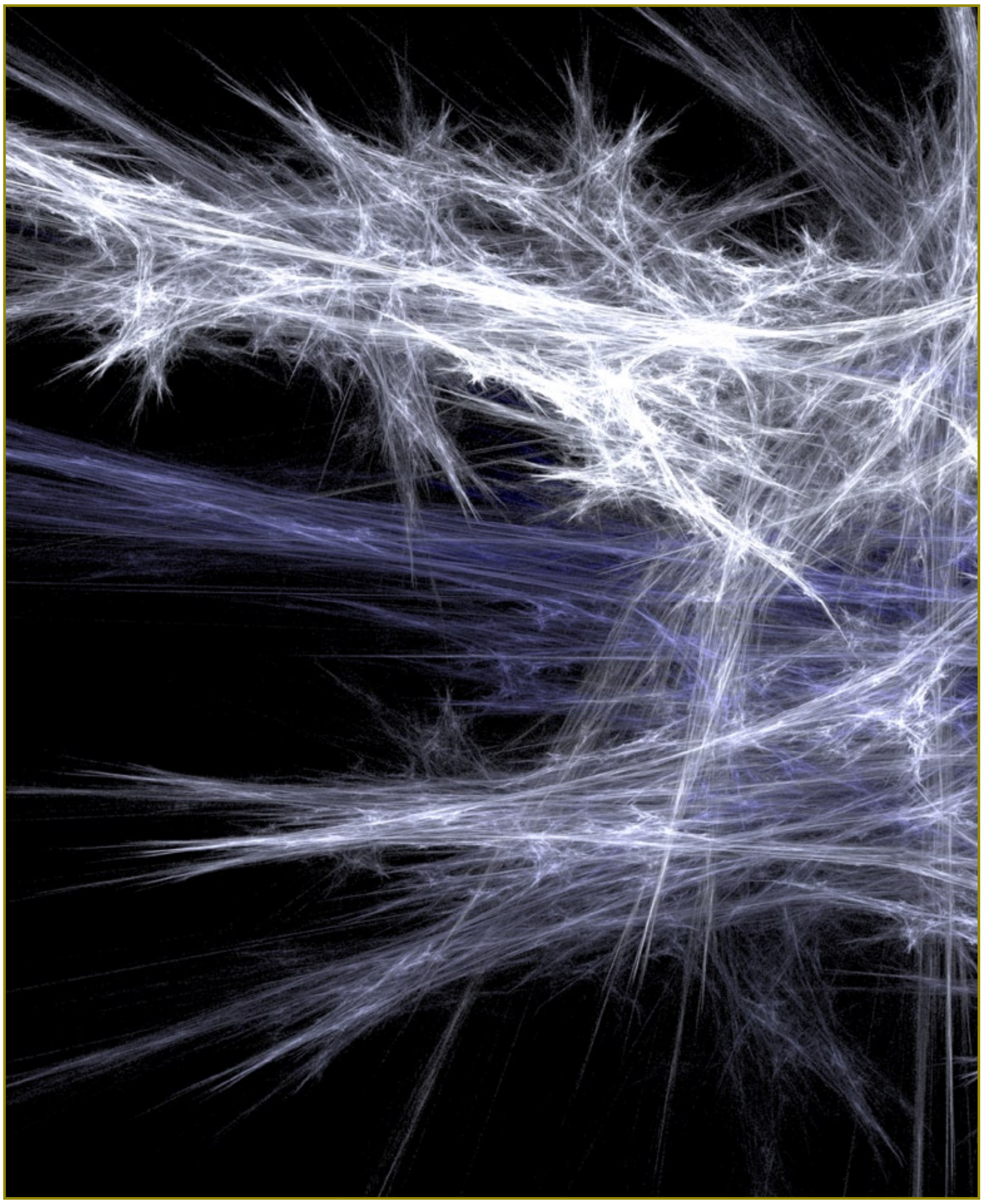

## 1. Executive Summary

Because neuroanatomy is a foundational aspect of neuroscience, workshop participants enthusiastically supported the creation of a standing International Coordinating Committee for Neuroanatomical Nomenclature (ICCNN). The mission of its respected experts would be to develop a widely accepted and freely accessible terminology for describing accurately the nervous system's structural organization at both the regional and cellular levels, based ultimately on an evolutionary/comparative approach. The final product should be implemented in a stepwise fashion and include a set of clearly defined terms and relationships between them that:

- is documented with scientific evidence and explanations
- supports alternate interpretations and terms
- provides updating and versioning in perpetuity.

The ICCNN should coordinate its work with atlas and web portal development, and with communities that are working independently on more restricted structural neuroscience problems, for example in insects or birds, or in particular regions like cerebral cortex within or across species. Finally, history suggests that for the resulting neuroanatomical terminology (ontology) to have lasting value, the ICCNN should articulate general principles underlying the schema used in its construction. Initially the ICCNN should survey existing resources and develop a prototype nomenclature on a tractable problem of wide basic and clinical interest like the vertebrate striatum.

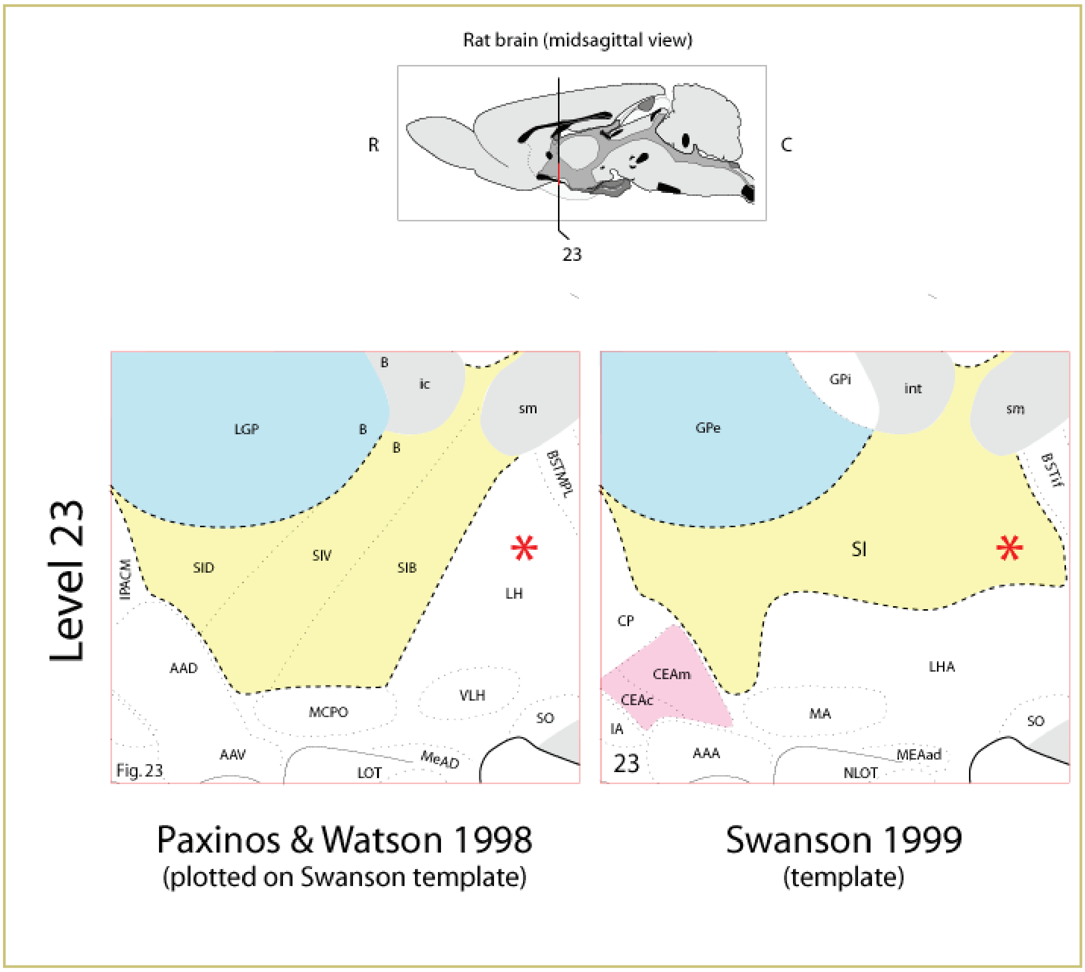


*Figure 1: A midsaggital view of the rat brain (up), mapped according to two parcellation schemes: Paxinos & Watson (1998) (left), and Swatson (1999). The big difference in parcellation schemes can lead to assignment of the same attribute, or function, to different brain regions (lateral hypothalamus and substantia innominata, respectively).*

## 2. Motivation

It is a tried and true principle that effective scientific communication relies on an accurate, defined vocabulary—and ultimately an accompanying linguistic medium—that is consistently applied. And in this day and age, databases and knowledge management systems drawing inferences from them require one or more sets of defined terms and relationships between the terms, both within and between the sets. Because neuroanatomy deals with the structural organization of the most complex object known—the brain and rest of the nervous system—the rigor of its terminology lags far behind that of other scientific disciplines. This is a great impediment to understanding and progress, and is due mainly to three factors: a complex and internally inconsistent literature that stretches back to classical antiquity and is expanding exponentially, a relative scarcity of data about many components that often precludes unambiguous conflict resolution, and the lack of a widely accepted theoretical framework for interpreting the data.

The vertebrate central nervous system (CNS) can be mapped in different ways depending on the techniques that have been applied, the sectioning angle, strains of animals, and the individual variability of animals. Last, but not least, the expertise of the neuroanatomists is another factor that heavily influences the process of CNS mapping. As a result, the CNS of many vertebrate species used in neuroanatomy, including humans, may be associated with different parcellation schemes provided by different authors.

The problem of many maps for a single species is not only important in itself, but it is also crucial in interpreting and integrating the results of any experiment performed in the vertebrate CNS. Any structural or functional variable that is measured in a specific experiment has to be mapped on a parcellation scheme. Therefore, the function assigned to a brain region depends heavily on the parcellation scheme that was used to map the experimental results. An often encountered example in mapping and interpreting experimental results provided by groups that use different schemes is shown in Fig. 1. The same situation applies to understanding the literature.

Another example that shows the high variability, depending on the mapping criteria, in parceling a restricted part of the brain is shown in Appendix A.

Even though the problem of many maps for a single species is very important for integrating different experimental results, and for understanding the literature, there is no systematic approach to indexing and relating parcellation schemes (to the best of our knowledge). The Brain Architecture Management System (BAMS; http://brancusi.usc.edu/bkms) that was presented at the workshop is one of the few existing neuroinformatics systems that handles information related to these problems (see also Appendix B).

As a conclusion, a systematic approach of the variety of maps in a single species is fundamental for the assignment of structure-function relationships of different parts of the vertebrate CNS.

# 3. Mission

Scientifically, the eventual goal is to provide an accurate descriptive framework for nervous system structural organization that is accepted broadly by the neuroscience community. This essential "skeleton" can be associated with functional and molecular data about each component, as well as with systems of interconnected components. Function at the molecular, cellular, systems, behavioral, and pathological levels is of paramount importance, but especially in the nervous system, which can be thought of as a complex biological computer; a combination of structural and functional approaches is the most effective approach to understanding, manipulation, and repair. The best example of integrated structure-function thinking in 20th century biology was the structural model of DNA proposed by Watson and Crick in 1953. It sparked the molecular biology revolution, and might inspire a similar revolution in 21st century systems neuroscience if a viable model of the nervous system's basic wiring diagram emerges. And for this, a clearly defined and broadly accepted structural vocabulary with relationships between terms/concepts (a computer science ontology) is one fundamental requirement.

Practically, it is customary to establish bases, principles, and rules for choosing the proper form of a preferred term and its definition—something that has not yet occurred for structural neuroscience. Based on a long history of similar exercises in other fields (like naming species and human macroanatomy), choices should be made on the preponderance of evidence as opposed to the force of authority, and priority of discovery should be honored whenever possible. Once the preferred set of parts has been chosen and defined, the next step involves classification and establishing hierarchies of parts, the art and science of taxonomy. Guiding principles used to develop a general or universal terminology for describing the structural organization of the nervous system can then be used for dealing with and coordinating more specialized topics or uses on both the neuroanatomy and computer science/artificial intelligence fronts. Examples might include particular species, periods of the life cycle, techniques (MRI, histochemical, and so on), parts or subsystems, and diseases. Bullock and Horridge (1965) provide a particularly good example of this general approach in Part I of their classic two-volume monograph.

# 4. Principles

A general approach to the long-term goal of developing a universal vocabulary for describing the nervous system's structural organization involves at least five basic steps. First, a comprehensive parts list needs to be assembled, including macroscopic and microscopic components—in other words, an account of regions and the pathways between them, as well as the neuron types and connections that form those regions and pathways. A good strategy would be to start with today's least controversial terms and work progressively toward the most ambiguous, and to provide references to the primary literature. Second, relationships between terms for parts in a particular species need to be established, which involves at least some aspects of classification. Based on intended use of the classification, this theoretical problem can be approached in multiple ways, all of which should be supported in a knowledge management system. Third, relationships between terms in different species need to be clarified, preferably on the basis of evolutionary and developmental considerations. Fourth, the parts can be arranged hierarchically, again in multiple, use-determined ways. Typically, the most general terms, applying to all species, appear at the top of a hierarchy, with specific terms for specific species appearing at the bottom. In addition, hierarchies may be developed from a top-down (monothetic, deductive) or a bottom-up (polythetic, inductive, hypothesis-driven) approach, or better yet, a combination of the two approaches, with the latter applied to lower levels of the hierarchy. Fifth, it is critical to facilitate continuous updating, alternate interpretations, and extensions in all aspects of the underlying knowledge management system.

Overall, however, the following distillation of experience should always guide deliberations. A good nomenclature or classification system is logical, practical, and easy to follow.

# 5. Recommendations

The seminal result of the workshop was enthusiastic endorsement at the end for the creation of a standing International Coordinating Committee for Neuroanatomical Nomenclature (or alternatively for Structural Neuroscience)—a formal vote was unanimous with one abstention. Committee implementation and operating procedures were left to the INCF's discretion. Obviously, the work of an International Coordinating Committee needs to be integrated into the INCF's Global Portal Services for the neuroscience community.

It is too early to make specific recommendations but the practical goals outlined here could serve as a guide for choosing expertise needed on the Committee, and as its initial working agenda.

## 5.1 Practical Goals of an International Coordinating Committee

Any committee that is established will, of course, determine its own specific goals, strategies, and timetables. However, these suggestions can serve as starting point for discussion.

*Short-term goals:*

- Survey existing general terminologies and knowledge management systems. Is there an existing system(s) adequate for general neuroanatomical nomenclature issues, combined with available "ontologies" or nomenclatures? Are there prototype ontologies that immediately could be implemented on, or linked to, the INCF Portal?

- Identify other groups working on specialized neuroanatomical nomenclature problems and help coordinate interactions among them.

- Facilitate development of an ideal "prototype" terminology for a problem of limited scope that could be expanded to the more general goals. One topic of widespread interest in the basic and clinical neurosciences, which could be approached from a broad comparative approach in vertebrates, is the striatum. For this it will be necessary to explicitly encode/specify criteria used for defining terms, and to develop a hierarchy of criteria.

- Consult with experts in the general fields of complex problem resolution and computer science.

- Develop a step-wise strategy for achieving medium-range and long-term goals.

*Medium-range goals:*

- Develop the universal set of terms for describing nervous system structural organization outlined above, based on traditional neuroanatomical nomenclature. In other words, extend the prototype(s) toward a hierarchical nomenclature schema applicable to particular species, and eventually to all species and stages of the life cycle.

- Begin acting as a resource for neuroanatomical nomenclature conflict resolution and clarification in the neuroscience community.

- Help serve as a quality control agent for online neuroanatomical nomenclature and classification resources, facilitating expert peer feedback.

*Long-term goals:*

- Consider developing a new, paradigm-shifting nomenclature and taxonomy for structural neuroscience (as accomplished long ago by Linnaeus and Darwin in other domains of the life sciences). This would involve a combination of empirical and theoretical approaches.

## 5.2 Other Life Science Nomenclature Efforts

Strategically, a great deal can be learned from other life sciences nomenclature committees. In anatomy, the pioneering effort emerged from a committee of the German Anatomical Society that deliberated and voted for almost a decade before publishing the *Basle Nomina Anatomica* (BNA) in 1895. It was influential because it 1) was done by a knowledgeable committee that limited the endeavor's scope (to human descriptive anatomy as seen with the naked eye or a hand lens), 2) employed a single language, and 3) elaborated rules for name assignment. Since then the BNA has undergone some half dozen revisions by international committees, and is now widely though not universally used in teaching human anatomy to medical students; the latest version is the *Terminologica Anatomica* (1998). However, this reference nomenclature, with its very simple and some would say old-fashioned hierarchical organization, has had little influence on experimental neuroanatomy, or on the nomenclature currently used in human brain MRI/PET studies.

Compared to species nomenclature, anatomical nomenclature—including that associated with the nervous system—is conservative and based on ancient traditions that emerged in classical antiquity. In fact, it is probably safe to say it is based on the surviving writings of Galen (second century AD) and Vesalius (1543). However, the broader topic of species naming underwent a revolution with the publication of Linnaeus's *Systema Naturae* (1735), where he advocated the use of a binominal nomenclature, with simply a general (genera) and specific (species) name for every taxon. His revolutionary concept was that a species name *labels* a concept rather than describes an entity, so that names or labels remain the same when definitions and descriptions change—in essence, names as such are insignificant and he did not hesitate to change them almost indiscriminately to fit the binominal plan. Names are simply a convenience for finding descriptions in lookup tables. In 1843 the British Association was the first to adopt a formal system for naming animal species, based on the work of a committee, and its recommendations had a widespread influence on nomenclatural practice. The keys to its success were 1) the goal of establishing a uniform, permanent language among naturalists of all nations, 2) no claim to mandatory authority or forceful sanctions, and 3) an explanation of why each article of the document was introduced. This document, the Stricklandian Code, has been continuously updated ever since, by a variety of national and international committees. Currently, the established moderator is the International Commission on Zoological Nomenclature (ICZN), which was established in 1895. Its stated mission is to insure that every animal (living and fossil) has one unique, universally accepted name. The product is a book of rules and procedures for naming species, the latest edition being published in 1998.

For the sake of completeness, it should at least be mentioned that Darwin (1859) revolutionized biological taxonomy with the concept that descent with modification is the natural organizing principle for establishing homologies; this is now accepted by all zoologists for animal taxonomy.

As a long-range goal, the ICCNN should at least bear in mind the possibility of fostering a paradigm-shifting nomenclature and taxonomy along the lines inspired by Linnaeus and Darwin. It should at least be easy to implement and compare with the more traditional approaches, in modern knowledge management systems.

# Appendix A

An example which illustrates the high variability —depending on the mapping criteria— when parcelling a restricted part of the brain, the frontal cortex of the macaque (ventral area 6). The same term used in different parcellation schemes does not automatically imply the identity of regions.

| Parcellation Scheme | Component Areas | Criteria |
|---|---|---|
| Brodmann, 1909 (B) | 6 | cytoarchitecture |
| Petrides & Pandya (P) | 6 | cytoarchitecture |
| | 44 | |
| Von Bonin & Bailey, 1947 (vB) | FBA | cytoarchitecture combined with myeloarchitecture |
| | FCBm | |
| von Bonin & Bailey, 1949 (vB, '49) | 44 | cytoarchitecture combined with myeloarchitecture |
| | 6 | |
| Vogt & Vogt (V) | 6a 6aα 6aβ | cytoarchitecture combined with myeloarchitecture |
| | 6b 6bα 6bβ | |
| | 4c | |
| Preuss & Goldman-Rakic (GR) | 6Va | cytoarchitecture combined with myeloarchitecture |
| | 6Vb | |
| | PrCO | |
| Barbas & Pandya (BP) | 6Va | cytoarchitecture combined with myeloarchitecture |
| | 6Vb | |
| | 4C | |
| Matelli et al. (M) | F4 | cytoarchitecture combined with chemoarchitecture (cytochrome oxidase staining) |
| | F5 | |
| Lewis & van Essen (vE) | 6Va 6Val 6Vam | cytoarchitecture combined with myeloarchitecture, and with chemoarchitecture (SMI-32 immunoreactivity) |
| | 6Vb | |
| | 4c | |
| | PrCO | |
| Petrides et al. (1999); Paxinos et al. (2000) | 6VC(F4) | cytoarchitecture combined with chemoarchitecture (several markers) |
| | 6VR(F5) | |
| | 44 | |
| | 45B | |

*Table 1: Macaque ventral area 6 equivalent parcellation schemes (Arbib and Bota, 2003).*

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# Appendix B

The Brain Architecture Management System (BAMS; http://brancusi.usc.edu/bkms) is one of the few existent neuroinformatics systems that takes a systematic approach to indexing and relating different parcellation schemes (Bota et al. 2005). BAMS includes 15 nomenclatures pertaining to 5 species (a total of more than 8800 terms), a module specifically designed for relating brain regions defined in different nomenclatures, and an inference engine for extracting 3D topological relations from qualitative relations established across pairs of Atlas Plates.

1 General approach: We have topologically compared the substantia innominata (SI) defined according the rat brain nomenclature Swanson-98 with a series of brain structures defined according the rat brain nomenclature Paxinos-Watson-98. We have compared the closest atlas levels in terms of distance from bregma, from the associated atlases, respectively. Collator: Mihail Bota Explanation

The inferred relations of Substantia innominata (SI), defined in Swanson-1998 are as follows:

overlaps with the ventral pallidum(VP), parcellation Paxinos/Watson-1998
overlaps with the lateral accumbens shell(LAcbSh), parcellation Paxinos/Watson-1998
overlaps with the accumbens nucleus, shell(AcbSh), parcellation Paxinos/Watson-1998
overlaps with the cell bridges of the ventral striatum(CB), parcellation Paxinos/Watson-1998
overlaps with the substantia innominata, basal part(SIB), parcellation Paxinos/Watson-1998
overlaps with the interstitial nucleus of the posterior limb of the anterior commissure(IPAC), parcellation Paxinos/Watson-1998
overlaps with the lateral preoptic area(LPO), parcellation Paxinos/Watson-1998
overlaps with the basal nucleus (Meynert)(B), parcellation Paxinos/Watson-1998
includes the substantia innominata, dorsal part(SID), parcellation Paxinos/Watson-1998
overlaps with the substantia innominata, ventral part(SIV), parcellation Paxinos/Watson-1998
overlaps with the lateral globus pallidus(LGP), parcellation Paxinos/Watson-1998
overlaps with the substantia innominata(SI), parcellation Paxinos/Watson-1998

Details of topological relations of Substantia innominata (SI), defined in Swanson-1998 as collated by Mihail Bota
In order to see the associated annotations for each of the established topological relation, go with the mouse over the relation.

| Structure(abbreviation) | Identified in: | Topological relation: | Atlas plate used for SI (Bregma) | Atlas plate used for related structure (Bregma) |
|---|---|---|---|---|
| ventral pallidum (VP) | Paxinos/Watson-1998 | overlap | 10 (+2.15) | 10 (+2.20) |
| | | overlap | 11 (+1.70) | 11 (+1.70) |
| | | overlap | 12 (+1.45) | 12 (+1.60) |
| | | overlap | 13 (+1.20) | 13 (+1.20) |
| | | covers | 14 (+0.95) | 14 (+1.00) |
| | | covers | 15 (+0.45) | 16 (+0.48) |
| | | covers | 16 (+0.10) | 17 (+0.20) |
| | | covers | 19 (-0.26) | 18 (-0.26) |
| | | overlap | 20 (-0.46) | 20 (-0.40) |
| | | overlap | 22 (-0.83) | 21 (-0.80) |
| | | covers | 23 (-1.08) | 22 (-0.92) |
| lateral accumbens shell (LAcbSh) | Paxinos/Watson-1998 | overlap | 10 (+2.15) | 10 (+2.20) |
| | | covers | 11 (+1.70) | 11 (+1.70) |
| | | overlap | 12 (+1.45) | 12 (+1.60) |
| | | overlap | 13 (+1.20) | 13 (+1.20) |
| | | overlap | 14 (+0.95) | 14 (+1.00) |
| accumbens nucleus, shell (AcbSh) | Paxinos/Watson-1998 | overlap | 12 (+1.45) | 12 (+1.60) |
| | | overlap | 13 (+1.20) | 13 (+1.20) |
| cell bridges of the ventral striatum (CB) | Paxinos/Watson-1998 | overlap | 14 (+0.95) | 14 (+1.00) |
| | | overlap | 15 (+0.45) | 16 (+0.48) |
| | | overlap | 16 (+0.10) | 17 (+0.20) |

*Figure 2: Output of the BAMS topological inference engine. Users can inspect the methodology for inserting topological relations employed by users, relations between different regions across corresponding sets of Atlas Levels, and inferred general relations between the related regions. For details, see Bota et al. 2005.*

## Appendix C: Workshop Program

September 10:

| | |
|---|---|
| 12:00-13:00 | Lunch |
| 13:00-18:00 | Scientific presentations and discussions |
| Larry W Swanson | Introduction – toward a global nervous system parts taxonomy |
| Nicolas J Strausfeldt & John G Hildebrand | Invertebrate nervous systems – general terms & principles |
| George Paxinos | Experience from a broad range of adult & developmental atlases |
| Anton J Reiner | The new avian brain nomenclature: a brief history |
| Sten Grillner | Basic conserved components of the vertebrate nervous system |
| Jürgen K Mai | Needs for human neuroanatomy |
| Harry B M Uylings | The problem of partial correspondences in a single species |
| Tom Smulders | Facilitating communication in comparative anatomy |
| Edward G Jones | Experience from the human & primate thalamocortical system |

September 11:

| | |
|---|---|
| 09:00-12:00 | Scientific presentations |
| Douglas M Bowden | Experience from NeuroNames |
| Maryann E Martone | Nomenclature needs of the Biomedical informatics Research Network (BIRN) |
| Mihail Bota | Constructing neuron nomenclatures & hierarchies in the Brain Architecture Knowledge Management System (BAMS) |
| 12:00-13:00 | Lunch |
| 13:00-17:00 | Draft report |

Each presentation was scheduled for 20 minutes, including questions.

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